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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/675,011	09/30/2003	Lynn Dickey	040989/267934	5538

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EXAMINER	
ZHENG, LI	

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/675,011	DICKEY ET AL.	
	Examiner	Art Unit	
	LI ZHENG	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *82-84 and 87-94* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *82-84 and 87-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/8/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 21, 2010 has been entered.

2. Claims 82-84 and 87-94 are pending and examined on the merits.

3. The rejections and objections not set forth in this action are withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 82-84 and 87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stomp et al. (1999, WO 99/07210) further in view of Wong et al. (1992,Plant Molecular Biology 20:81-93), Buzby et al. (1990, The Plant Cell 2:805-814) and Stiekema et al. (1983, Nucleic Acid Research 11:8051-8061).

The instant claims are drawn to a stably transformed duckweed plant culture or duckweed nodule culture wherein said plant culture or nodule culture is transformed with one or more nucleotide sequences comprising a coding sequence for a biologically active polynucleotide , an operably linked coding sequence for a signal peptide that directs secretion of said polypeptide and an operably linked 5' leader sequence consisting of SEQ ID NO: 6; or wherein said culture is from Lemna gibba, or wherein said biologically active polypeptide is an antibody.

Stomp et al. teach a method of producing a biologically active recombinant polypeptide (page 9, lines 1-9) in a duckweed culture, where the nucleotide sequence comprising the coding sequence for the polypeptide is operably linked to a coding sequence for a signal peptide (page 12, lines 16-23) that directs secretion of the polypeptide into the culture medium (page 12, lines 16-23, and claim 49), and collecting the biologically active recombinant polypeptide from the culture medium (claim 49). Stomp et al. also teach producing a biologically active recombinant polypeptide where the polypeptide is encoded by nucleotide sequence that has been modified for enhanced expression in duck weed (page 15, lines 18-28), a biologically active multimeric protein including mAb, hemoglobin, P450 oxidase and a mAb (page 9, lines

1-9, also claim 48 and 52), a mammalian polypeptide (page 9, lines 16-21), a therapeutic polypeptide (page 8, lines 2-5), a human growth hormone and alpha interferon (page 8, lines 16-19, also claim 12, 47 and 56). Stomp et al. also teach that the expression cassette may further contain 5' leader sequence to enhance translation (page 12, lines 3-15). Stomp et al. further teach that the transit peptide from duckweed L. gibba isolated by Stiekema et al. can be used as transit polypeptide for enhancing translation.

Stomp et al. do not teach 5' leader sequence from RbcS gene, 5' leader sequence SEQ ID NO: 16 or signal peptide that directs secretion being from rice α-amylase set forth by SEQ ID NO: 6.

Buzby et al. (1990, The Plant Cell 2:805-814) teach upstream sequences of three RbcS genes from L. gibba, including the 5' leader sequence from RbcS 5B gene which encompasses SEQ ID NO: 16.

Wong et al. teach the 5' leader sequence from RbcS gene of Arabidopsis.

It would have been obvious to a person with ordinary skill in the art to modify the method of Stomp et al. by utilizing the 5' leader sequence of Buzby et al. from L. gibba. One would have been motivated to do so given the teaching of Stomp et al. that the expression cassette may further contain 5' leader sequence to enhance translation, the teaching of Wong et al. that the 5' leader sequence from RbcS gene of Arabidopsis can enhance expression of GUS activity (page 89, 2nd paragraph of right column). Furthermore, a 5' leader sequence of a RbcS gene from a duckweed L. gibba becomes an obvious choice given that the expression host is also a duckweed. The resulting

modified method of Stomp et al. would obviously produce claimed stably transformed duckweed.

5. Claims 82-84 and 87-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stomp et al. (1999, WO 99/07210) further in view of Wong et al. (1992,Plant Molecular Biology 20:81-93), Buzby et al. (1990, The Plant Cell 2:805-814), and Stiekema et al. (1983, Nucleic Acid Research 11:8051-8061) as for claims 82-84 and 87, further in view of Hein et al. (US Patent Number 5,959,177).

Claims 88-92 further contain limitations such as wherein said antibody is expressed from one or more nucleotide sequences comprising a coding sequence for a chain of the antibody; or wherein the duckweed culture expresses and assembles a heavy chain and light chain of the antibody; or wherein the antibody is Fab' fragment or monoclonal antibody or a human antibody.

The combined teaching of Stomp et al. in view of Wong et al. (1992,Plant Molecular Biology 20:81-93), Buzby et al. (1990, The Plant Cell 2:805-814), and Stiekema et al. (1983, Nucleic Acid Research 11:8051-8061) are discussed above. The combined teachings do not teach wherein said antibody is expressed from one or more nucleotide sequences comprising a coding sequence for a chain of the antibody; or wherein the duckweed culture expresses and assembles a heavy chain and light chain of the antibody; or wherein the antibody is Fab' fragment or monoclonal antibody or a human antibody. .

Hein et al. teach expression of expression human antibody (Table B), Fab fragment, heavy chain and light chain of antibody (columns 3-4; also claim 7)

It would have been obvious to a person with ordinary skill in the art to modify the method of Stomp et al. in view of Wong et al. (1992,Plant Molecular Biology 20:81-93), Buzby et al. (1990, The Plant Cell 2:805-814), and Stiekema et al. (1983, Nucleic Acid Research 11:8051-8061) by expression heavy chain and light chain or Fab fragment of human antibody according to teaching of Hein et al. One would have been motivated to make such modification given the teaching of Hein et al. that mammalian antibody can be generated and assembled in plants by the method of Hein et al. (claims 1-12; abstract).

6. Claims 82-84 and 87-94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stomp et al. (1999, WO 99/07210) further in view of Wong et al. (1992,Plant Molecular Biology 20:81-93), Buzby et al. (1990, The Plant Cell 2:805-814), Stiekema et al. (1983, Nucleic Acid Research 11:8051-8061) and Hein et al. (US Patent Number 5,959,177) as for claims 82-84 and 87-92, further in view of Yu et al. (1995, U.S. Patent No. 5460952) and Park et al. (1997, The Journal of Biological Chemistry 272:6876-6881).

Claims 82-84 and 87-92 are discussed above.

Claims 93-94 further contain a limitation that the signal peptide comprises SEQ ID NO: 6 encoded by SEQ ID NO: 3.

The combined teaching of Stomp et al. in view of Wong et al. (1992,Plant Molecular Biology 20:81-93), Buzby et al. (1990, The Plant Cell 2:805-814), and

Stiekema et al. (1983, Nucleic Acid Research 11:8051-8061) and Hein et al. (US Patent Number 5,959,177) are discussed above.

The combined teachings of Stomp et al. in view of Wong et al. (1992,Plant Molecular Biology 20:81-93), Buzby et al. (1990, The Plant Cell 2:805-814), and Stiekema et al. (1983, Nucleic Acid Research 11:8051-8061) and Hein et al. (US Patent Number 5,959,177) do not teach signal peptide that directs secretion being from rice α-amylase set forth by SEQ ID NO: 6 encoded by SEQ ID NO: 3.

Yu et al. teach a rice α-amylase comprising a signal peptide set forth by SEQ ID NO: 6 (SEQ ID NO: 3 nucleotides 2366-2458).

It would have been obvious to a person with ordinary skill in the art to further modify the method of Stomp et al. in view of Wong et al. (1992,Plant Molecular Biology 20:81-93), Buzby et al. (1990, The Plant Cell 2:805-814), and Stiekema et al. (1983, Nucleic Acid Research 11:8051-8061) and Hein et al. (US Patent Number 5,959,177) by using the signal peptide of Yu et al. as a signal polypeptide for secretion. One would have been motivated to do so given the teaching of Yu et al. that secretion into media of the plant cell cultures is a potential commercial source of medicines (column 1, lines 45-65) and the teaching of Park et al. that signal peptide from rice α-amylase can be recognized and processed by various expression systems including yeast Y. lipolytica (at least abstract).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 82-84, 87 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-17 of U.S. Patent No. 6,815,184 (hereafter '184) in view of Wong et al. (1992,Plant Molecular Biology 20:81-93), and Buzby et al. (1990, The Plant Cell 2:805-814).

Claims 16-17 of '184 are drawn to a method of producing biologically active α-2b-interferon in a duckweed plant culture or a duckweed nodule culture and the stably transformed duckweed produced. Claims 16 and 17 also teach a secretion signal polypeptide is operably linked to the interferon gene. SEQ ID NO: 3 in claim 16 of '184 encodes a rice α-amylase signal polypeptide of SEQ ID NO: 6.

Claims 16-17 of '184 do not teach 5' leader sequence from RbcS gene.

Buzby et al. (1990, The Plant Cell 2:805-814) teach upstream sequences of three RbcS genes from L. gibba, including the 5' leader sequence from RbcS 5B gene which encompasses SEQ ID NO: 16.

Wong et al. teach the 5' leader sequence from RbcS gene of Arabidopsis.

It would have been obvious to a person with ordinary skill in the art to modify the method of instant claims of '184 by utilizing the 5' leader sequence of Buzby et al. from L. gibba. One would have been motivated to do so given the teaching of Wong et al. that the 5' leader sequence from RbcS gene of Arabidopsis can enhance expression of GUS activity (page 89, 2nd paragraph of right column). Therefore a 5' leader sequence of a RbcS gene from a duckweed L. gibba becomes an obvious choice given that the expression host is a duckweed. The resulting modified method would obviously produce claimed stably transformed duckweed.

Applicants traverse in the paper filed 5/21/10. Applicants' arguments have been fully considered but were not found persuasive.

Applicants argue that '184 does not contemplate or disclose the use fo 5' leader sequence of SEQ ID NO: 16 while Buzby et al. provide no teaching as to the use of SEQ ID NO: 16 as a translation enhancer sequence. Applicants further argue that Wong et a. teach that effect of a RbcS 5' untranslated leader on heterologous protein expression is unpredictable (response, the paragraph bridging pages 9-10).

The Office contends that Wong et a. do not teach that effect of a RbcS 5' untranslated leader on heterologous protein expression is unpredictable because

variability in efficacy is not considered as being unpredictable. On the contrary, given the general knowledge that 5' leader sequence from various RbcS genes can be used to enhance expression in plants (e.g. leader sequence from soybean Rbcs as taught in US Patent Number 6,329,574) with different efficacy, it would further motivate a person skilled in the art to choose a duckweed 5' UTL from RbcS gene to enhance the heterologous gene expression in a duckweed host.

8. Claims 82-84 and 87-94 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of US Patent Number 7,632,983 (hereafter '983). Claim 1 of '983 is drawn to a method of producing a recombinant monoclonal antibody having effector's function in a duckweed plant culture or a duckweed nodule culture, comprising the steps of:

(a) culturing within a duckweed culture medium a duckweed plant culture or a duckweed nodule culture, wherein said duckweed plant culture or said duckweed nodule culture is stably transformed to express said monoclonal antibody, and wherein said monoclonal antibody is expressed from one or more nucleotide sequences comprising a coding sequence for a chain of the monoclonal antibody, an operably linked coding sequence for a signal peptide that directs secretion of the monoclonal antibody, an operably linked 5' leader sequence of SEQ ID NO: 16 of instant application, and an operably linked plant intron sequence that is inserted upstream of the coding sequence; and

(b) collecting said antibody from the duckweed culture medium, the duckweed plant culture, or the duckweed nodule culture, wherein said coding sequence for the chain of

the monoclonal antibody comprises between 70-100% Lemna gibba-preferred codons or Lemna minor-preferred codons.

Claim 8 of '983 further limits a signal peptide being SEQ ID NO: 6 of instant application. Therefore the claims of '983 teaching all the limitations set forth in the instant claims.

Applicants do not present any argument and therefore the rejection is maintained. However, Applicants' intention to address the filing of a terminal disclaimer when the application is otherwise in condition for allowance is acknowledged (response, page 11, 2nd paragraph from the bottom of the page).

11. Claims 82-84 and 87 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 11/778,480 (hereafter '480) in view of Wong et al. (1992,Plant Molecular Biology 20:81-93), and Buzby et al. (1990, The Plant Cell 2:805-814).

Claim 2 of '480 is drawn to The duckweed plant culture or duckweed nodule culture of claim 1,wherein said nucleic acid molecule has at least one attribute selected from the group consisting of:

(a) duckweed-preferred codons in the coding sequence for said α-2b-interferon peptide;

(b) duckweed-preferred codons in the coding sequence for said signal

(c) a translation initiation codon that is flanked by a plant-preferred translation initiation context nucleotide sequence, wherein said plant-preferred translation initiation context

nucleotide sequence consists of the nucleotide sequence "ACC" or "ACA", wherein said context is positioned immediately adjacent to of the 5' end of the translation initiation codon;

(d) an operably linked nucleotide sequence comprising a plant intron that is inserted upstream of the coding sequence; and

(e) an operably linked 5' leader sequence.

Claim 21 further limit the signal polypeptide being rice α-amylase signal peptide set forth of SEQ ID NO: 6 of instant application.

Claims of '480 does not specify the 5' leading sequence being the one from RbcS gene.

Buzby et al. teach upstream sequences of three RbcS genes from L. gibba, including the 5' leader sequence from RbcS 5B gene which encompasses SEQ ID NO: 16.

Wong et al. teach the 5' leader sequence from RbcS gene of Arabidopsis.

It would have been obvious to a person with ordinary skill in the art to modify the method of instant claims of '184 by utilizing the 5' leader sequence of Buzby et al. from L. gibba or 5' leader sequence from RbcS gene of Arabidopsis of Wong et al. One would have been motivated to do so given the teaching of Wong et al. that the 5' leader sequence from RbcS gene of Arabidopsis can enhance expression of GUS activity (page 89, 2nd paragraph of right column). Furthermore, a 5' leader sequence of a RbcS gene from a duckweed L. gibba becomes an obvious choice given that the expression

host is a duckweed. The resulting modified method would obviously produce claimed stably transformed duckweed.

This is a provisional obviousness-type double patenting rejection.

Applicants do not present any argument and therefore the rejection is maintained. However, Applicants' intention to address the filing of a terminal disclaimer when the application is otherwise in condition for allowance is acknowledged (response, page 10, 3rd paragraph from the bottom of the page).

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Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Li Zheng/
Examiner, Art Unit 1638